TITLE: Development of stable **lyophilized** monoclonal **antibody** formulations: Effect of excipients on stability.

AUTHOR(S): Bam, Narendra; Dal Monte, Paul R.; Duddu, Sarma P.
CORPORATE SOURCE: Pharm. Dev., SmithKline Beecham Pharm., King of Prussia, PA 19406 USA

SOURCE: Abstracts of Papers American Chemical Society, (1996) Vol. 211, No. 1-2, pp. BIOT 143.
Meeting Info.: 211th American Chemical Society National Meeting New Orleans, Louisiana, USA March 24-28, 1996
ISSN: 0065-7727.
DOCUMENT TYPE: Conference
LANGUAGE: English

AN 2977694 IFIPAT;IFIUDB;IFICDB
TITLE: DRY COMPOSITIONS FOR PREPARING SUBMICRON EMULSIONS; **LYOPHILIZED**; CRYOPROTECTANTS; EMULSIFIERS; OIL IN WATER EMULSION

INVENTOR(S): Aldouby, Yanir, Modiin, IL
Friedman, Doron, Karmei-Yosef, IL
PATENT ASSIGNEE(S): Pharmos Corporation, New York, NY

PRIMARY EXAMINER: Kishore, Gollamudi S
AGENT: Pennie & Edmonds

	NUMBER	DATE
PATENT INFORMATION:	US 5750142	19980512
APPLICATION INFORMATION:	US 1997-840177	19970411
EXPIRATION DATE:	12 Feb 2013	

	APPLN. NUMBER	DATE	GRANTED PATENT NO. OR STATUS
CONTINUATION OF:	US 1995-486791	19950607	ABANDONED
DIVISION OF:	US 1993-16913	19930212	5472706

	NUMBER	DATE
PRIORITY APPLN. INFO.:	IL 1992-101007	19920218
FAMILY INFORMATION:	US 5750142	19980512
	US 5472706	

DOCUMENT TYPE: UTILITY
FILE SEGMENT: CHEMICAL
NUMBER OF CLAIMS: 39

AB The present invention relates to dry, stable compositions which can be

reconstituted to form pharmaceutical or cosmetic emulsions, and to methods for making such compositions. An emulsion is formed from about 0.2 to 25 weight percent of a first component of an oil, about 0.1 to 5 weight percent of a second component of an emulsifier, about 0.25 to 25 weight percent of a cryoprotectant of an amino compound, such as one or more amino acids, peptides or protein hydrolysates, and an aqueous component, wherein the amino compound is present in an amount that is equal to or greater than that of the first component. Optionally, a co-emulsifier, a suspension agent, a preservative, an antioxidant and a drug can be added to these emulsions. Thereafter, the emulsion is lyophilized to form dry compositions that have from about 40 to about 90 weight percent of the amino compound; from about 0.1 to about 20 weight percent of the emulsifier; and from about 0.2 to about 40 weight percent of the oily component. By combining the dry composition with an appropriate quantity of an aqueous liquid, the composition is reformed as an oil-in-water emulsion.

ACCESSION NUMBER: 1999:292570 CAPLUS
DOCUMENT NUMBER: 130:329204
TITLE: Process for producing dry, amorphous products comprising biologically active materials by convection drying, especially spray drying
INVENTOR(S): Gabel, Rolf-Dieter; Mattern, Markus; Winter, Gerhard; Wirl, Alexander; **Woog, Heinrich**
PATENT ASSIGNEE(S): Roche Diagnostics G.m.b.H., Germany
SOURCE: Eur. Pat. Appl., 21 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 913177	A1	19990506	EP 1997-119112	19971103
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
EP 913178	A1	19990506	EP 1998-120455	19981029

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO

NO 9805096	A	19990504	NO 1998-5096	19981102
AU 9890459	A1	19990520	AU 1998-90459	19981102
JP 11228389	A2	19990824	JP 1998-311629	19981102

PRIORITY APPLN. INFO.: EP 1997-119112 19971103

AB A soln. or suspension of a biol. active material (e.g. protein) and a stabilizing mixt. of a carbohydrate and a zwitterion with a polar or nonpolar group (e.g. an amino acid), or .gtoreq.2 zwitterions or derivs. thereof, is subjected to convection drying at a relative humidity of <70% and an inlet air temp. of <300.degree. to produce an amorphous or partially amorphous, homogeneous powd. product comprising uniform (esp. spherical) particles and having a glass transition temp. .gtoreq.20.degree. (preferably .gtoreq.40.degree.) and a residual moisture content <8%. The product is stable for .gtoreq.12 mo and has a d. .gtoreq.15% higher than that of **lyophilizates**. Thus, a mixt. of sucrose (50 mg/mL), L-arginine (10 mg/mL), and L-phenylalanine (10 mg/mL) was spray dried at an inlet air temp. of 100.degree.. The product had residual water content 3.2%, d. 1.023 g/cm3, and glass transition temp. 57.6.degree..

ACCESSION NUMBER: 1995:867872 CAPLUS
DOCUMENT NUMBER: 123:266155
TITLE: Pharmaceutical preparation containing plasminogen activators
INVENTOR(S): Kohnert, Ulrich; Fischer, Stephan; Markl, Hans-joerg; **Woog, Heinrich**
PATENT ASSIGNEE(S): Boehringer Mannheim GmbH, Germany
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9522347	A1	19950824	WO 1995-EP596	19950218

W: AU, BG, BR, BY, CA, CN, CZ, EE, FI, HU, JP, KR, KZ, LT, LV, MX, NO, NZ, PL, RO, RU, SI, SK, UA, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

CA 2183755	AA	19950824	CA 1995-2183755	19950218

AU 9517581	A1	19950904	AU 1995-17581	19950218
AU 691881	B2	19980528		
EP 746334	A1	19961211	EP 1995-910500	19950218
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
CN 1141592	A	19970129	CN 1995-191732	19950218
HU 74843	A2	19970228	HU 1996-2284	19950218
BR 9506840	A	19971014	BR 1995-6840	19950218
JP 09511495	T2	19971118	JP 1995-521599	19950218
ZA 9501371	A	19960820	ZA 1995-1371	19950220
FI 9603251	A	19960820	FI 1996-3251	19960820
NO 9603460	A	19961018	NO 1996-3460	19960820
US 5747030	A	19980505	US 1996-693226	19960821
PRIORITY APPLN. INFO.:			DE 1994-4405426	19940221
			WO 1995-EP596	19950218

AB Stable, water-sol. pharmaceutical prepns. contg. plasminogen activators, sugar, and tranexamic acid (solubilizer) as a **lyophilizate** or as an injection or infusion soln. are described. The prepns. contain in particular a sugar, a phosphate buffer, tranexamic acid, and a surfactant, the pH of the liq. solns. preferably being 5.5-6.5, and do not cause adverse effects on the veins.

ACCESSION NUMBER: 1994:62044 CAPLUS
DOCUMENT NUMBER: 120:62044
TITLE: Stabilization of drugs by freeze drying; **lyophilization** in nonaqueous solutions as well as optimization of freeze drying processes
AUTHOR(S): **Woog, Heinrich**
CORPORATE SOURCE: Abt. TP-GP, Boehringer Mannhein GmbH, Mannheim, 68261, Germany
SOURCE: Paperback APV (1993), 35(Lyophilisation), 39-60
CODEN: PPRBDN; ISSN: 0720-3543
DOCUMENT TYPE: Journal; General Review
LANGUAGE: German
AB A review with 7 refs.

ACCESSION NUMBER: 1990:124967 CAPLUS
DOCUMENT NUMBER: 112:124967
TITLE: Pharmaceutical development of **lyophilizates**
AUTHOR(S): **Woog, H.**
CORPORATE SOURCE: Boehringer Mannheim G.m.b.H., Mannheim, Fed. Rep. Ger.
SOURCE: Pharma Technol. J. (1989), 10(3), 14-24
CODEN: PTJOEH
DOCUMENT TYPE: Journal; General Review
LANGUAGE: German
AB A review with no published refs. discussing drug stabilization by freeze-drying, optimization of development of **lyophilizates**, preformulation, scaling-up and validation.

AN 2703913 IFIPAT;IFIUDB;IFICDB
TITLE: PROCESS FOR THE PRODUCTION OF MULTI-DOSE PHARMACEUTICAL PREPARATIONS CONTAINING ISOLATED OR RECOMBINANTLY PRODUCED HUMAN PROTEIN FOR INFUSION OR INJECTION PURPOSES; DISSOLVING PRESERVATIVES IN AQUEOUS SOLUTIONS OF PURIFIED PROTEINS OR KITS CONTAINING SEPARATE PACKAGES OF FREEZE DRIED PROTEINS

INVENTOR(S): Demmer, Fritz, Hirschberg, DE
Gruber, Werner, Birkenau, DE
Markl, Hans-Jorg, Ellerstadt, DE
Winter, Gerhard, Dossenheim, DE
Woog, Heinrich, Laudenbach, DE
PATENT ASSIGNEE(S): Boehringer Mannheim GmbH, Mannheim, DE
PRIMARY EXAMINER: Chan, Christina Y
ASSISTANT EXAMINER: Degen, Nancy J
AGENT: Nikaido, Marmelstein, Murray & Oram

	NUMBER	DATE	
PATENT INFORMATION:	US 5503827	19960402	
	(CITED IN 004 LATER PATENTS)		
	WO 9303744	19930304	
APPLICATION INFORMATION:	US 1994-193002	19940215	
	WO 1992-EP1822	19920810	
		19940215	PCT 371 date
		19940215	PCT 102(e) date

EXPIRATION DATE: 2 Apr 2013

	NUMBER	DATE
PRIORITY APPLN. INFO.:	DE 1991-4126983	19910815
FAMILY INFORMATION:	US 5503827	19960402

DOCUMENT TYPE: UTILITY
FILE SEGMENT: CHEMICAL
MICROFILM REEL NO: 007093 FRAME NO: 0832
NUMBER OF CLAIMS: 66

AB The present invention concerns a process for the production of well-tolerated, preserved injection or infusion solutions containing human protein.